REMARKS

Claims 47 - 62 are pending in the application. Claims 22, 25 - 30, and 32 - 46 are canceled herein. New claims 47 - 62 are herein added. No new matter is added by these amendments.

At the outset, Applicants submit that new claims 47-62 are substantially similar to claims 22, 25-30, and 36-46, and are presented for greater clarity. In particular, the following chart shows the relationships between these newly presented claims and the previous claims:

New claim (Presented Herein)	**Claim previously presented**
47	27
48	28
49	29
50	26
51	38
52	39
53	40
54	41
55	42
56	30
57	32
58	43
59	33
60	44
61	34
62	46

Applicants submit that claims 22, 25, 35-37, and 45 are cancelled and not reintroduced in the new claims presented herewith, and as explained in more detail below.

Objections to the Specification

The Examiner objected to the disclosure of the invention because the amendment on March 14, 2002, changing the word "structural" to "structured" on page 10, line 1, was allegedly found to be confusing.

Applicants submit that this amendment was made to correct a typographical error in the first sentence of page 10. Applicants submit that this amendment is not confusing because the same amended language is used elsewhere in the specification (e.g., page 10, line 16). Therefore, Applicants respectfully request that this objection be withdrawn.

Rejections under 35 USC §101

Claims 22, 25-30 and 32-46 were rejected under 35 USC §101 because the claimed invention is allegedly not supported by either a specific or substantial utility or a well established utility. Specifically, the Examiner takes the position that the specification does not appear to show a structured panel of peptides that can be used to identify a target-binding peptide

or any other kind of target-binding molecules. Applicants respectfully traverse this rejection.

Page 71 of the specification discloses use of a number of different phage libraries, and Applicants submit that this constitutes a structured panel of peptides. Applicants submit that the specification at page 71 discloses ten separate libraries, each containing peptides made from (5 amino acids)-(constant amino acid)-(5 amino acids). Ten different libraries, each with a different fixed residue were produced, and these different libraries were screened against UL44. The results are shown on pages 73 and 74 of the specification, and indicated that peptides from two different libraries were found to bind UL44 and GSTUL44. Applicants submit that this data shows that a panel of different biased combinatorial linear peptide libraries have been used to identify previously unknown target binding peptides, and thus shows evidence of utility under 35 USC §101.

Claim 47 (formerly claim 27) recites:

> A structured panel consisting of a plurality of biased combinatorial linear peptide libraries, each library comprising a plurality of different peptides, all peptides of said panel being of the same length, there being one and only one amino acid in a fixed position in said peptides which is both (1) for each library, the same amino acid (a

"constant" amino acid) in all peptides of that library, and (b) not the same amino acid in all libraries of said panel, said position being fixed for all peptides in all libraries of said panel, wherein said fixed position is (a) at least five residues from both ends of the peptides or (b) in the middle 50% of the peptides, shown by the formula

$$(Xaa)_m\text{-}R1\text{-}(Xaa)_n$$

wherein R1 is the amino acid at said fixed position, and m and n do not differ by more than two,

wherein each library is a separate and physically distinct entity from all other libraries of the panel, and

wherein the peptides are displayed on viruses.

Applicants submit that the Example shown on page 71 et seq. shows a structured panel, (i.e., a panel where there is some structural relationship between the member libraries, with a constrant residue being at the same position). Each library comprises a plurality of different peptides with all the peptides being the same length, there being one and only one position in the peptide which is both (1) for each library the same amino acid (a constant amino acid) in all peptides of that library and (2) not the same amino acid in all libraries of the panel. That is, the constant residue is in the same position, but the panel comprises ten different libraries, each with a different constant residue. Furthermore, the fixed position is

at least five residues from the end of the peptides and is also within the middle 50% of the peptides. Each peptide is also a separate, physically distinct entity from the other libraries of the panel (because it has a different constant residue).

Furthermore, at page 9, last paragraph, the specification defines a panel of combinatorial libraries as a collection of different, although possibly overlapping, and separately screenable simple or composite combinatorial libraries. A panel differs from the compositie library in that the component simple libraries have not been mixed together, (i.e., they may be screened separately. Applicants submit that the Example shown on page 71 also meets these requirements.

Accordingly, Applicants submit that the presently claimed invention discloses a specific and credible utility as demonstrated on pages 71-73 contrary to the Examiner's assertion, and therefore meets the utility requirements of 35 USC §101. Applicants therefore submit that this rejection is overcome.

Rejections under 35 USC §112, first paragraph

Claims 22, 25-30 and 32-46 were rejected under 35 USC §112, first paragraph for various reasons. Specifically, the Examiner first indicates that the specification does not provide support

for the term "middle 50%". Applicants submit that the originally filed disclosure at page 25, lines 35 - 38, states "[p]referably, AA_1 is located at or near the center of the peptide. More preferably AA_1 is either (a) at least five residues from both ends of the peptide or (b) is in the middle 50% of the peptide." Applicants submit that other statements made in the specification that have been previously pointed out to the Examiner illustrate sufficient disclosure to warrant the term "middle 50%." Accordingly, Applicants submit this rejection has been overcome and request the Examiner to withdraw the rejection.

The Examiner also asserted that the specification does not provide a written description for the claimed structured panel of library and a peptide wherein the constant residue is "***within*** the middle 50%." The Examiner states that the disclosure does not describe how a structured panel can be made from a plurality of libraries, how the plurality of library form or structured into a panel or the minimum or maximum limit of the plurality contained in any one of the panel and a constant residue that is within 50% of the sequence.

Applicants have canceled claims 22, 25 - 30 and 30 - 46 and have presented new claims 47 - 62. The newly presented claims have been amended to recite "in the middle 50%." As stated in

Applicants' comments above, this terminology is supported by the originally filed specification. Applicants submit that this terminology is consistent with the terminology used in the specification and claims of the application, and therefore Applicants submit this rejection is overcome.

Additionally, the Examiner states the disclosure does not describe what constitutes a subpanel of a panel or a panel with more than two biased residue positions. Applicants submit that the disclosure provides support for subpanels of a panel with more than two biased residue positions on at least page 10, lines 9-32. Specifically, Applicants note that the disclosure states that one may have structured panel of libraries in which one may define subpanels too. Additionally, beginning on page 27 at line 25, the specification discloses holding two residues constant in a library.

The Examiner also stated that the specification does not provide support for "a plurality of biased combinatorial linear peptide libraries" as recited in claim 27 (now claim 47). In response, Applicants draw the Examiner's attention to page 9, lines 9-12 which defines a biased combinatorial library as one in which, at one or more positions in the library member, only one of the possible basic elements is allowed for all members of the library, i.e., the biased positions are invariant.

Additionally, Applicants draw the Examiner's attention to page 10, lines 1-8 which defines "structured panel" as a panel where there is some structural relationship between the member libraries." Applicants submit that these definitions along with the entirety of the specification provide disclosure and support to overcome the instant rejection.

Further, the Examiner stated that the entire claims 32-35, 39 and 43-46 do not have support in the specification. The Examiner lists several examples, i.e., plurality of residue positions other than said first position and the proviso "where if said libraries comprise more than two constant residue positions, the constant residue positions other than said first and second positions are constant for all peptides in said panel." Also, the Examiner points out "where said panel comprises a plurality of subpanel" in claim 32 and "subset of a set" in claim 33.

Applicants submit that the specification provides support for the phrase "plurality of residue positions" throughout the entirety of the specification. Applicants submit that on page 25 of the specification, beginning at line 15, "Peptide Libraries" are described. The specification states that a peptide library is a combinatorial library, at least some of whose members having three or more amino acids connected via

peptide bonds. Additionally, at line 27 a formula is recited showing a plurality of residues. Accordingly, Applicants submit that the disclosure provides support for a plurality of residues in a structured panel of biased combinatorial linear peptide libraries.

Applicants also submit that the specification provides adequate disclosure for libraries comprising more than two constant residue positions the constant residue positions other than the first and second positions are constant for all peptides in said panel. Specifically, support for holding two residues constant can be found at least on page 27, lines 25-38 and page 28, page 29. Additionally, support for this phrase can be found in the initially filed claims.

Applicants further submit that support for the term "subpanel" as used in the claims can be found on at least page 10, lines 16 - 20 which states that "one may have structured panels of libraries in which one may define subpanels, too. For example, in one subpanel, the middle residue AA_1 may be the same for all libraries, but the libraries also have a constant residue AA_2 which is scanned through all other residue portions." Applicants also submit that one skilled in the art would understand, from reading the disclosure as a whole, the meaning

of the term subpanel. Therefore, Applicants submit there is adequate support in the specification for the term "subpanel."

Applicants submit that the disclosure supports the phrase "subset of a set." Specifically, the disclosure provides support in the originally filed claims.

Claims 22, 25-30 and 32-46 were rejected under 35 USC §112, first paragraph, as failing to comply with the enablement requirement. Specifically the Examiner stated that the specification does not teach how to make a structured panel. Applicants submit that the specification discloses a method of making and using a panel at pages 25 - 37 which, *inter alia*, describes the preparation and use of peptide libraries of the present invention. Additionally, the Applicants draw the Examiner's attention to Example 1, particularly pages 70 - 78 which, *inter alia*, describes such libraries. One skilled in the art would understand that the explanation of preparation and use of libraries as disclosed in the present specification comports with the preparation and utilization of the claimed structured panel. Accordingly, Applicants submit that these rejections have been overcome, and respectfully request that the Examiner withdraw these rejections.

Rejections under 35 USC §112, second paragraph

Claims 22, 25-30 and 32-46 are rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, claims 32 and 33 were rejected as allegedly not pointing out what is included or excluded by the expression "a subset of the set of amino acids allowed at the remaining positions of said library" or a panel as a whole or " a panel comprising a plurality of subpanels, each comprising a plurality of libraries, and in each subpanel, the location of the second position is constant."

Page 10, lines 16 - 20 states that "one may have structured panels of libraries in which one may define subpanels, too." The specification additionally states in one subpanel, the middle residue AA_1 may be the same for all libraries, but the libraries also have a constant residue AA_2 that is scanned through al other residue positions. Therefore, a panel of libraries may also include a subpanel of libraries.

Claim 27 was rejected as being indefinite with regards to the term "fixed." The Examiner suggested Applicants recite a formula in claim 27 to overcome this rejection. Accordingly Applicants herein cancel claim 22 and have included such a

formula in new claim 47 presented herein, and thank the Examiner for this suggestion.

Claims 25, 30, 32, 33 and 35 were rejected under 35 USC §112 second paragraph for various reasons. Claim 25 was rejected as being inconsistent or at odds with claim 30. Applicants herein cancel claim 25 and now submit that this rejection is moot.

Claim 30 was rejected because the definition of R "is the amino acid at said first fixed position" allegedly provides for confusion and ambiguity. Applicants herein cancel claim 30 and present new claim 56 which is substantially similar. Newly presented claim 56 recites "wherein R1 is the amino acid at said first fixed position, and m and n do not differ by more than two, and wherein R1 is selected from tryptophan, proline or tyrosine." Accordingly, Applicants submit that the instant rejection has been overcome. Therefore, Applicants request that the Examiner withdraw the rejection.

Additionally, claim 30 was rejected to because the definition of m and n do not differ by two is contradictory to the preceding statement of either (a) or (b). Applicants submit that claim 30 recites that "in each library, said fixed position is (a) at least five residues from both ends of the peptides or (b) within the middle 50% of the peptides . . . ." Accordingly,

the library must have at least five residues from both ends of the peptides, or must have a fixed position within the middle 50% of the peptides. Thus indicating that the fixed position is not an end position in the library.

Moreover, to utilize the Examiner's example of m=0 and n=2, R1 (the fixed position) will not be at least five residues from each end of the peptides, nor would it be within the middle 50% of the peptides. Accordingly, peptides of the formula suggested by the Examiner will not fall within the scope of the claim. Therefore, Applicants submit that this rejection has been overcome and respectfully request the Examiner to withdraw the instant rejection.

Claim 32 was rejected as being confusing as to the "plurality of subpanels." The Examiner states that it is unclear as to the plurality of libraries contained in a plurality of subpanels contained in a panel.

Applicants herein cancel claim 32 and present new claim 57. Applicants submit that newly presented claim 57 is not confusing as to the "plurality of subpanels." As stated in Applicants comments above, support for such subpanels can be found at least on page 10, lines 16-20. Applicants submit that a structured panel is made of member libraries. A panel could have subpanels with a subpanel having a middle residue AA_1 that is the same for

the libraries of that subpanel. Applicants submit that this claim does not go beyond the original disclosure as this recitation was presented as at least original claim 19.

Claim 35 was rejected to as being indefinite as to the characterization of the compound by the method by which the library is made. Applicants herein cancel claims 35 and 36, 37, and 45. No corresponding newly presented claims are submitted herein. Accordingly, Applicants submit that this rejection has been rendered moot.

Rejections under 35 USC §102

Claims 32 - 38 were rejected under 35 USC §102(a) as being anticipated by Pinilla et al. (U.S. Patent No. 5,556,762). Applicants respectfully traverse the rejection.

Pinilla discloses six separate pluralities as sets of oligopeptides. Each set is a mixture of oligopeptide chains that contain six amino acid residues. Each set differs by having a different predetermined amino acid at the same predetermined position. The remaining amino acid positions of the peptide chain in the set have equimolar amounts of at least ten different amino acid residues at the other positions. Thus, Applicants understand that each set in the Pinilla reference is a mixture of different peptides, and each has the same amino

acid at the same fixed position. Thus, different sets have different amino acids at the same fixed position.

Further, Pinilla discloses different pluralities of sets, that is, Pinilla uses an additional group of sets with a mixture of oligopeptides. Each of those sets has the fixed position at a different point in the oligopeptide chain. This can be summarized as follows:

Different Sets

Set 1	Set 2
ABODEF	ABPDEG
CDOGHI	CEPGHI
GHOCDA	GAPABC

Different Plurality of Sets

Set 3	Set 4
ABDOEF	ABDPEG
CDGOHI	CEGPHI
GHCODA	GAAPBC

Applicants herein cancel claims 32 - 38 and present substantially similar new claims 51, 52, 57, 59 and 61. Newly presented claims 51, 52, 57, 59 and 61 recite, among other things, "[a] structured panel of biased combinatorial linear peptide libraries, each library comprising a plurality of different peptides, all peptides of said panel being the same

length, each library having at least two constant residue positions, one at a first position and the other at a second position. . . ."

Applicants submit that the Pinilla reference does not disclose or suggest an amino acid at a second fixed position. The Applicants disagree with the Examiner that the Pinilla reference discloses the presently claimed invention as recited in newly presented claims 51, 52, 57, 59, and 61 (canceled claims 32 - 38).

Therefore, Applicants submit that the newly presented claims are not anticipated by the Pinella reference, and that this rejection is overcome.

Rejections under 35 USC §103

Claims 22, 25-30, 38-40 and 42 are rejected under 35 USC §103(a) as being obvious over U.S. Patent No. 5,532,167 (Cantley et al.) in view of Pinilla et al. Applicants respectfully traverse this rejection.

Pinilla et al. is discussed above. The Examiner states that Cantley et al. discloses a degenerate peptide library which is a population of peptides in which different amino acid residues are present at the same position in different peptides within the library.

Applicants submit that Cantley et al. discloses a method for determining an amino acid sequence motif for a phosphorylation site of a protein kinase. While Applicants do agree that Cantley et al. discloses a polypeptide library that has a constant, fixed amino acid, Applicants disagree that Cantley et al. discloses or suggests a structured panel consisting of a panel of libraries. In Cantley et al., the amino acid is selected from serine, threonine, and tyrosine. There are a number of variable amino acids on each side of this fixed amino acid. Specifically, there are between one and ten amino acids on each side of the fixed amino acid.

Applicants note that the Cantley et al. reference identifies four degenerate residues on each side of the fixed amino acid, and note that a preferred example shows 6 residues on one side of the fixed amino acid and 8 residues on the other side of the fixed amino acid.

Claims 22, 25 - 30, 38 - 40 and 42 are herein canceled and presented in substantially similar new claims 47 - 53, 55, and 56. In contrast to the disclosure of the Pinilla and Cantley et al. references, newly presented claims 47 - 53, 55, and 56 recite, among other things, the use of a structured panel comprising a plurality of biased combinatorial libraries. Applicants submit that the Cantley et al. reference does not

disclose a structured panel comprising a plurality of biased combinational libraries since only one library at a time is disclosed within the reference.

Applicants submit that neither the Pinilla nor the Cantley et al. references taken alone or together disclose or suggest the use of a structured panel comprising a plurality of biased combinatorial libraries.

Applicants submit that the instant rejection has been overcome and accordingly request the Examiner to withdraw the rejection.

Claims 22, 25 - 30, 39 - 40 and 42 were rejected under 35 USC §103(a) as being obvious over Sparks et al. (U.S. Patent No. 6,303,574) in view of Pinilla.

The Examiner submits that Sparks et al. discloses a phage-displayed random peptide having at least 9 and up to 45 amino acid residues. The Examiner lists several 13-mer peptides that include Proline as a middle portion residue. The Examiner additionally states that Pinilla discloses mixtures of peptides in which individual residue position can be specifically defined such that a comprehensive array of peptides is available for the identification of one or more of the optimal peptides for reaction with receptors of interest. The Examiner concludes

that it would have been obvious to make the different libraries of Sparks into a panel for the advantages bought by Pinilla.

Applicants respectfully traverse the rejection. Applicants submit that Sparks et al. discloses peptides having general and specific binding affinities for the Svc homology region 3 (SH 3) domains of proteins. However, Applicants disagree with the Examiner that Sparks et al. discloses a library as it is defined in the instant specification. Sparks discloses a mixture of different random peptides. Some of the peptides have a middle protein residue, while others do not. Accordingly, Applicants submit that the peptides cannot be considered as a library as defined in the current invention. (See pages 8-10 of the instant specification.)

Claims 22, 25 - 30, 39 - 40 and 42 are herein canceled and are presented in substantially similar new claims 47 - 53, 55, and 56. Applicants submit that the newly presented claims recite, among other things, "a structured panel consisting of a plurality of biased combinatorial linear peptide libraries . . . ." The Sparks et al. and Pinilla references do not disclose or suggest a structured panel as disclosed and claimed in the current application.

The present inventiors have found that most peptides need structure to have sufficiently high affinity for a particular

target for the peptides to be selective and useful. It has been found that peptides with a fixed proline or a fixed cysteine are more useful than those having a fixed glycine. Accordingly, a peptide of the present invention is more improved than what has been previously disclosed in the art. Therefore, the currently claimed invention is not rendered obvious by Sparks et al. which discloses a random library, in view of Pinilla et al. Applicants therefore submit the instant rejection has been overcome and respectfully request the Examiner to withdraw the rejection.

Applicants now submit that the application is in condition for allowance, and reconsideration and a timely Notice of Allowance is earnestly solicited.

If the Examiner believes a telephone conference would aid in the continued prosecution of this application, the Examiner is invited and encouraged to contact Applicants' representative at the telephone number listed below.

Any fees due with this Reply may be charged to Deposit Account **23-1665** under Customer Number **27267**.

Respectfully submitted,

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